RESPONSES TO APPENDIX M-I-C-1
HUMAN GENE TRANSFER PROTOCOLS

RECOMBINANT DNA ADVISORY COMMITTEE MEETING
June 2001

ID #	Letter	Protocol #	Response
		9905-315	**A Phase I/II Study of a Prime-Boost Schedule of Human GM-CSF Gene Transduced Irradiated Prostate Allogeneic Cancer Vaccine (Allogeneic Prostate GVAX TM) in Hormone-Refractory Prostate Cancer (G9803) . Sponsor: Cell Genesys, Inc.**
107	3/16/2001		*Response to M-I-C-1:* Received a response under Appendix M-I-C-1 of the NIH Guidelines (Jan. 2001), for the amendment (reported at the March 2001 RAC meeting) to enroll a single individulal. This latest submission provided a copy of the IRB final approval, IRB-approved informed consent, and clinical protocol. Readministration of the study reagent was initiated on February 22, 2001.
		0001-381	**Gene Therapy of Canavan Disease using AAV for Brain Gene Transfer.**
144	3/22/2001		*Response to M-I-C-1:* This submission from Dr. Paola Leone (Assistant Professor, Department of Neurosurgery, Thomas Jefferson University), dated March 22, 2001 to the file for RAC protocol #0001-381, addresses the recommendations and observations of the Recombinant DNA Advisory Committee (RAC) regarding this protocol made during the public discussion at the March 2000 RAC meeting and outlined in an April 18, 2000 letter from Dr. Amy Patterson. In additon a facsimile from Thomas Jefferson University dated April 9, 2001 was received in which a typographical error in the lead letter of the March 22, 2001 submission is corrected. This typographical error does not impact on the contents of the responses to the RAC recommendations and observations.

ID #	Letter	Protocol #	Response
		0005-399	**An Open-Label, Phase I, Dose-Escalation Study of Tumor Necrosis Factor-alpha (TNFeradeTM Biologic) Gene Therapy with Radiation Therapy for Locally Advanced, Recurrent, or Metastatic Solid Tumors. Sponsor: GenVec**
51	2/22/2001		*Response to M-I-C-1:* a. Change in the list of investigators. One of the principal investigators, Dr. Jigna Desai Jhaveri from the Albert Einstein College of Medicine, will be replaced by Dr. Anand Sharma from the same institution. The reason for this change was not given. In addition, Dr. Nader Hanna at the University of Kentucky Medical Center has been added as a PI.
		0006-402	**Phase I Study to Evaluate the Safety of Cellular Immunotherapy for Recurrent/Refractory Neuroblastoma Using Genetically-Modified Autologous CD8+ T Cell Clones.**
123	4/26/2001		*Response to M-I-C-1:* Received a response under Appendix M-I-C-1 of the NIH Guidelines (Jan. 2001), providing a copy of the IBC, IRB final approvals, IRB-approved informed consent, and clinical protocol approved by the IBC and IRB. Investigator has indicated that trial was initiated on February 22, 2001. Summary of changes made to the clinical protocol as required by the FDA: 1) eligibility criteria have been consolidated in appendix B 2) exclusion criteria have been revised to include ganciclovir intolerance 3) protocol has been revised "...to specify the target dose and acceptable dose range for starting cell product and for hygromycin-selected cell clones."
		0007-409	**A Phase I, Multi-Center, Open-Label, Dose-Escalation Study of the Safety and Tolerability of Intravenously Administered VLTS-587 in Patients with Solid Tumors and the Presence of Metastases or Primary Cancer in the Lungs. Sponsor: Valentis, Inc.**
122	2/23/2001		*Response to M-I-C-1:* Received a response under Appendix M-I-C-1 of the NIH Guidelines (Jan. 2001) for the Sarah Cannon Cancer Center site, providing a copy of the IBC, IRB final approvals, IRB-approved informed consent, and clinical protocol approved by the IBC and IRB. Sponsor has indicated that first individual was consented on January 24, 2001. However, this individual did not receive study medication; individual met an exclusion criterion. No additional individuals have been consented as of this date.

ID #	Letter	Protocol #	Response	
		0010-419	**Intratumoral Injections of a Replication-Incompetent Adenoviral Vector Encoding a Factor VII Immunoconjugate to Induce a Cytolytic Immune Response against Melanoma Tumors: A Pilot Trial.**	
145	2/20/2001		*Response to M-I-C-1:*	An amendment to protocol #0010-419 was submitted to OBA on February 20, 2001 by the principal investigator, Dr. Albert Deisseroth of Yale University School of Medicine. In this submission, Dr. Deisseroth addresses the concerns raised by the RAC at the December 15, 2000 meeting and which were summarized in Dr. Patterson's letter from January 2, 2001. The concerns raised, and Dr. Deisseroth's responses, can be placed into the following categories: 1. Potential safety concerns of abnormal bleeding and disseminated intravascular coagulation (DIC) due to a reaction to either the adenoviral vector or to the immunoconjugate containing the mutated factor VII targeting domain. 2. Additional biodistribution studies should be done so as to verify that this product will selectively bind to tumor vasculature and not normal vasculature. 3. The stopping rules should be tightened up so that ANY death would lead to a full review of all patients' data. 4. For the 3rd and 4th cohorts, the second and subsequent patients should only be enrolled once there has been the establishment of the safety of this new dosing regimen in the initial patient in each group. 5. Changes in the informed consent forms and issues of paying for the medical treatment of adverse events believed to be secondary to the study compound. A new study protocol was submitted as well as a revised Appendix M.
		0011-431	**A Phase II Study of High-Dose Allovectin-7 in Patients with Advanced Metastatic Melanoma. Sponsor: Vical Inc.**	
50	3/ 2/2001		*Response to M-I-C-1:*	Received a response under Appendix M-I-C-1 of the NIH Guidelines (Jan. 2001), for the Missouri Baptist Medical Center/Melanoma Center of St. Louis. Copies of IBC and IRB approvals, informed consent, and indication that this site was open for enrollment was on March 5, 2001. Copy of clinical protocol was also submitted.
49	3/ 9/2001		*Response to M-I-C-1:*	Received a response under Appendix M-I-C-1 of the NIH Guidelines (Jan. 2001), for the Univ. of Colorado Health Sciences site (PI: Dr. Gonzalez). Copies of IBC and IRB approvals, informed consent, and indication that this site was open for enrollment on February 7, 2001. Copy of clinical protocol was submitted previously on March 2, 2001.

ID #	Letter	Protocol #	Response
		0011-432	**A Phase II Study of Safety and Efficacy of Allovectin-7 Immunotherapy for the Treatment of Primary Resectable Squamous Cell Carcinoma of the Oral Cavity or Oropharynx. Sponsor: Vical Inc.**
120	2/28/2001		*Response to M-I-C-1:* Received a response under Appendix M-I-C-1 of the NIH Guidelines (Jan. 2001), providing a copy of the IBC, IRB final approvals, IRB-approved informed consent for the University of Cincinnati site. Clinical protocol approved by the IBC and IRB was previously submitted on November 15, 2000. This site is open for research participant enrollment as of February 7.
		0011-435	**Vaccination in Peripheral Stem Cell Transplant Setting for Multiple Myeloma: The Use of Autologous Tumor Cells with an Allogeneic GM-CSF Producing Bystander Cell Line. Sponsor: Cell Genesys, Inc.**
126	5/ 3/2001		*Response to M-I-C-1:* Received a response under Appendix M-I-C-1 of the NIH Guidelines (Jan. 2001), providing a copy of the IBC, IRB final approvals, IRB-approved informed consent. The protocol submitted for RAC review is the latest version. Sponsor has indicated that first individual was enrolled on April 9, 2001. *Page 4 of 4*